AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0008] on page 3 of the Specification with the following:

The ~~inventors have~~ inventor has observed in clinical studies that UARS patients are known to exhibit one or more of the aforementioned symptoms/signs found in patients with functional somatic syndromes. In particular, UARS patients often exhibit one or more symptoms/signs common to functional somatic syndromes, including, but not limited to, sleep-onset insomnia, headaches, irritable bowel, gastroesophageal reflux (i.e., heartburn), depression, bruxism, and alpha-delta sleep. Other symptoms/signs found in UARS patients include rhinitis, hypothyroidism, and asthma.

Please replace paragraph [0009] on page 3 of the Specification with the following:

In view of the foregoing, the similarity in symptoms/signs between UARS and FSS patients has led the ~~inventors~~ inventor to conclude that unrecognized inspiratory airflow limitation during sleep, such as that which takes place in UARS, likely plays a role in the development of functional somatic syndromes. Specifically, the frequent arousal and alpha wave intrusion into sleep of patients with functional somatic syndromes and the nonrestorative sleep associated with functional somatic syndromes is likely the result of impaired inspiratory airflow during sleep. Thus, treatment of inspiratory airflow limitation during sleep is likely to be effective in treating functional somatic syndromes. Additionally, the symptoms/signs associated with functional somatic syndromes may be useful in diagnosing sleep disorders such as OSA/H and UARS. Accordingly, one object of the present invention is to provide a method of treating functional somatic syndromes by correcting inspiratory airflow limitation during sleep. Another object of the present invention is to provide a method of treating functional somatic syndromes that overcomes the shortcomings of conventional treatment techniques aimed at treating the individual symptoms/signs of functional somatic syndromes. A further object of the present

invention is to provide a method of diagnosing sleep disorders, such as OSA/H and UARS, based on symptoms/signs commonly associated with functional somatic syndromes.

Please replace paragraph [0020] on page 6 of the Specification with the following:

As indicated previously, both OSA/H and UARS patient manifest several similar outward symptoms, including snoring, fitful sleep, and daytime sleepiness/fatigue. Additionally, as indicated previously, the ~~inventors have~~ inventor has observed that UARS patients share one or more symptoms/signs found in patients with functional somatic syndromes. In particular, UARS patients often exhibit one or more symptoms/signs common to functional somatic syndromes, including sleep-onset insomnia, headaches, irritable bowel, gastroesophageal reflux (i.e., heartburn), depression, bruxism, and alpha-delta sleep. FIG. 1 is a chart comparing the prevalence of these particular symptoms/signs in patients with OSA/H with the prevalence of the same symptoms/signs in patients with UARS, as well as other symptoms/signs associated with these sleep disorders. FIG. 1 illustrates the general higher prevalence of functional somatic syndrome symptoms in UARS patients than OSA/H patients. However, FIG. 1 further illustrates that, while UARS patients exhibit a higher percentage of certain functional somatic syndrome symptoms/signs than do OSA/H patients, OSA/H patients (either mild/moderate or moderate/severe) also exhibit at least these particular symptoms/signs associated with functional somatic syndromes. Thus, the ~~inventors have~~ inventor has determined that the symptoms/signs associated with functional somatic syndromes may be used as a key to identifying both OSA/H and UARS sleep disorders in accordance with the present invention. Moreover, the present invention applies the ~~inventors'~~ inventor's discovery of the similarity of symptoms/signs associated with UARS and functional somatic syndromes as a basis for treating functional somatic syndromes.

Please replace paragraph [0022] on page 7 of the Specification with the following:

Polysomnograms of UARS and OSA/H patients indicate that OSA/H patients demonstrate inspiratory airflow of less than fifty percent of waking levels associated with oxyhemoglobin desaturation. Patients with UARS have less severe inspiratory flow limitation, such as an inspiratory airflow of approximately fifty-one to one hundred percent of waking levels, due to a less collapsible upper airway. In both cases, inspiratory airflow is limited to some degree, and it is this limitation that is believed by the ~~inventors~~ inventor to be a contributing cause in the development of functional somatic syndromes. Specifically, the frequent arousal and alpha wave intrusion into sleep of patients with functional somatic syndromes and the non-restorative sleep associated with functional somatic syndromes is believed by the ~~inventors~~ inventor to be a result of impaired inspiratory airflow during sleep. Thus, treatment of inspiratory airflow limitation during sleep is likely to be effective in treating functional somatic syndromes.

Please replace paragraph [0035] on page 11 of the Specification with the following:

The ~~present inventors~~ inventor conducted a study in which seventy-five patients (75) with UARS and OSA/H were selected for the study. Twenty-five (25) UARS patients had an apnea/hypopnea index (AHI) of less than 10/h. Twenty-five (25) patients had mild to moderate OSA/H and an AHI of greater than or equal to 10/h but less than 40/h. Twenty-five (25) patients had moderate to severe OSA/H and an AHI greater than or equal to 40/h.

Please replace paragraph [0041] on page 12 of the Specification with the following:

During the nasal CPAP study, each patient slept wearing a nasal CPAP mask available commercially from Respironics, Inc., Murrysville, Pa. The mask was attached via a breathing circuit and a bi-directional valve to a pressure support system capable of administering

a positive airway pressure, such as a CPAP device, and to a source of negative pressure, such as a modified REMstar.RTM. brand CPAP unit also commercially available from Respironics, Inc. Using the dual pressure sources, the ~~present~~ inventor was able to vary the mask pressure between -20 cm H.sub.2O and 20 cm H.sub.2O. The monitoring of sleep stages, leg movements, heart rhythm, and oxyhemoglobin saturation during the nasal CPAP study was the same as for polysomnography.

Please replace paragraph [0045] on page 14 of the Specification with the following:

To ensure a broad range of sleep-disordered breathing severity in the patients, the inventor collected 25 consecutive patients at each of three levels of severity of AHI UARS (AHI less than ~~10/r~~ 10/h), mild-to-moderate OSA/H (AHI less than or equal to 10 to less than 40/h), and moderate-to-severe OSA/H (AHI less than or equal to 40/h). Each patient's questionnaires, history, physical examination, and polysomnogram were reviewed to abstract the needed information. Whenever it was determined that information was missing, the physician who performed the consultation obtained the missing information during the next clinical contact (usually within one month of polysomnography). The designation of symptoms/signs as "present" or "absent" according to the criteria listed above was done by individuals blinded to the severity of the patient's sleep-disordered breathing.

Please replace paragraph [0054] on page 16 of the Specification with the following:

To evaluate whether the symptoms/signs whose prevalence were greatest in patients with UARS were widely distributed among those patients, or whether they were clustered in a small group of patients with numerous symptoms/signs, the ~~present~~ inventor chose five symptoms/signs that tended to be most prevalent in patients with UARS, including sleep-onset insomnia, headache, IBS, alpha-delta sleep, and bruxism (FIG. 1), and counted the

frequency of these symptoms/signs in each patient with sleep-disordered breathing. It was found that the five symptoms/signs tended to be widely distributed among patients with UARS. More than 96% of the patients with UARS had at least one symptom/sign, with 72% having from two to four symptoms/signs. Despite their decreased prevalence, the symptoms/signs were also widely distributed among patients with OSA/H, with 64% having at least one symptom/sign. Thus, the symptoms/signs that tended to be more prevalent in patients with UARS were broadly distributed among patients with sleep-disordered breathing and not just clustered in a small subset of patients with numerous symptoms/signs.

Please replace paragraph [0056] on pages 16-17 of the Specification with the following:

The foregoing example further suggests that the continuum of upper airway collapsibility during sleep characterizes sleep disordered breathing causing different types of sleep disorders. For example, a high degree of inspiratory flow limitation during sleep is associated with moderate to severe OSA/H, while a lesser inspiratory flow limitation is associated with UARS. The use of an airway stabilization technique, whether a mechanical stabilization technique or a stabilization technique incorporating positive airway pressure therapy will address the symptom/signs of OSA/H or UARS and, therefore, the symptoms/signs of functional somatic syndrome. As indicated previously, the ~~inventors believe~~ inventor believes that the frequent arousal and alpha wave intrusions into the sleep of patients with functional somatic syndromes and the non-restorative sleep associated with these syndromes may result from this inspiratory flow limitation. Treatment of inspiratory flow limitation may thus correct or modify the symptoms of functional somatic syndromes.

Please replace paragraph [0057] on page 17 of the Specification with the following:

To further confirm the hypothesis regarding treating functional somatic syndromes through airway stabilization techniques, the ~~inventors'~~ inventor conducted an additional study specifically on female fibromyalgia patients. Generally, the object of the study was to determine whether fibromyalgia patients have inspiratory airflow dynamics during sleep comparable to female UARS patients. The patients included twenty-eight (28) female fibromyalgia patients diagnosed by rheumatologists using established criteria. Fourteen (14) of the patients gave a history of snoring, while four (4) claimed to snore occasionally, and ten (10) denied snoring. The comparison group included eleven (11) female UARS patients matched for age and obesity. Eighteen (18) of the twenty-eight (28) fibromyalgia patients and all the UARS patients had a full-night polysomnogram. All patients had a nasal CPAP study with quantitative monitoring of inspiratory airflow and effort between atmospheric pressure and therapeutic CPAP. Fourteen (14) fibromyalgia patients and all UARS patients had a successful determination of pharyngeal critical pressure (Pcrit). Of the twenty-eight (28) female fibromyalgia patients, twenty-seven (27) had sleep disordered breathing. One patient of the twenty-seven (27) had obstructive sleep hypopnea (OSA/H), while twenty-six (26) of twenty-seven (27) patients had milder inspiratory airflow limitation with arousals. One (1) patient exhibited no OSA/H or inspiratory airflow limitation during sleep. While sleeping at atmospheric pressure, apnea/hypopnea index, arousal index, the prevalence of airflow limited breaths, and maximal and inspiratory airflow were comparable between groups. The Pcrit of female fibromyalgia patients was -6.5.+-.3.5 cmH.sub.2O (mean.+-.SD) compared to -5.8.+-.3.5 cmH.sub.2O for female UARS patients (p=0.62). Treatment of fourteen (14) consecutive patients with nasal CPAP resulted in an improvement in functional symptoms ranging from 23% to 47% as assessed by a validated questionnaire. The results of this additional study indicate that inspiratory airflow limitation during sleep likely plays a primary role in the development of the functional somatic syndromes. Further details of the study are provided hereinafter.

Please replace paragraph [0059] on page 18 of the Specification with the following:

As indicated previously, a study sample of twenty-eight (28) pre-diagnosed female fibromyalgia patients took part in the ~~inventors~~ inventor's CPAP study. The twenty-eight (28) female fibromyalgia patients were required to complete a detailed medical and sleep related questionnaire before being evaluated by a physician board-certified in both Internal Medicine and Sleep Medicine. The physician performed a general medical and sleep-related history. As indicated previously, full-night polysomnography was performed using standard methodology. Airflow at the nose and mouth was monitored with a thermocouple. Thoracoabdominal movement was monitored with piezoelectric belts. Oxyhemoglobin saturation was monitored at the finger using a pulse oximeter. Sleep was staged using the scoring system of Rechtschaffen and Kales with the modification of Flagg and Coburn for sleep disordered breathing. The presence of alpha-delta sleep was identified by the characteristic low frequency (<2 cycles/s) high amplitude (>75 microvolt peak to trough) delta waves with superimposed 7-11 cycle/s alpha waves. EEG arousals not associated with hypopnea or apnea were identified using the American Sleep Disorders Association Atlas Task Force criteria. For each patient, the total of arousals not associated with hypopnea or apnea was divided by the total sleep time to derive an arousal index (arousals/hr). The apnea/hypopnea index (AHI) was quantified for each patient. The diagnosis of OSA/H was established by an AHI of at least 10 events/hour sleep.

Please replace paragraph [0062] on pages 19-20 of the Specification with the following:

While breathing at atmospheric pressure during the nasal CPAP study, twenty-six (26) of the twenty-seven (27) fibromyalgia patients without OSA/H experienced inspiratory airflow limitation during NREM sleep. The ~~present~~ inventor sampled 61.+-.17 consecutive breaths at atmospheric pressure per patient and found a prevalence of airflow limited breaths of 90.+-.13%. Therefore, inspiratory airflow limitation was the prevalent breathing pattern during

sleep among the female fibromyalgia patients. The mean maximal inspiratory airflow for the fibromyalgia patients with inspiratory airflow limitation was 169.+-.90 ml/s and the mean inspiratory change in esophageal pressure was 13.+-.9 cmH.sub.2O. The therapeutic CPAP pressure was 7.+-.2 cmH.sub.2O. At the therapeutic pressure, the mean inspiratory esophageal pressure for the group was 6.+-.5 cmH.sub.2O representing a 7 cmH.sub.2O decrease in inspiratory effort from a mask pressure of atmospheric pressure. The nasal CPAP findings confirm that the 30.0.+-.13.7 arousals/hr experienced by the eighteen (18) fibromyalgia patients who underwent full-night polysomnography were respiratory event related arousals (RERA's).

Please replace paragraph [0063] on page 20 of the Specification with the following:

The upper airway airflow dynamics during sleep of the female UARS patients were comparable to those of the female fibromyalgia patients. Compared to the female fibromyalgia patients, the female UARS patients had similar values of AHI and arousal index. Their values of maximal inspiratory airflow under conditions of inspiratory airflow limitation during NREM sleep were similar. Their values of therapeutic pressure were similar. There were statistically non-significant trends toward a lower esophageal pressure and a higher calculated resistance upstream to the site of airflow limitation in the fibromyalgia patients compared to the UARS patients. The ~~present~~ inventor sampled 58.+-.18 consecutive breaths at atmospheric pressure per female UARS patient and found a prevalence of low limited breaths of 91.+-.12% (a prevalence nearly identical to that of the female fibromyalgia patients).

Please replace paragraph [0066] on page 21 of the Specification with the following:

Each of the foregoing examples relate to studies on a sample of patients with one or more functional somatic syndromes. The inventor's second study concentrated on a specific functional somatic syndrome, fibromyalgia. Each of the studies demonstrates that a high

prevalence of inspiratory airflow limitation during sleep accompanies the functional somatic syndromes. The second study (Example II) firmly demonstrated that treatment with nasal CPAP improves functional symptoms in fibromyalgia patients. In particular, nasal CPAP treatment improves functional symptoms when inspiratory airflow limitations are prevented with nasal CPAP. Each of these examples supports the ~~inventors'~~ inventor's conclusion that inspiratory airflow limitation during sleep plays a primary role in development of the functional somatic syndromes, and treatment with an airway stabilization technique in accordance with the present invention improves the symptoms/signs associated with the functional somatic syndromes.